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Evaluation of late-onset sepsis antibiotic utilization and revision of empiric late-onset sepsis antibiotic prescribing guidelines

Alex Creevan
Providence St. Joseph Health, Portland, OR, Alexandre.Creevan@providence.org

Sara Clark
Providence St. Joseph Health, Portland, OR, sara.clark@providence.org

Anavice Jimenez
Providence St. Joseph Health, Portland, OR, Anavice.Jimenez@providence.org

Michael Garcia
Providence St. Joseph Health, Portland, OR, Michael.Garcia3@providence.org

Evaluation of late-onset sepsis antibiotic utilization within two tertiary healthcare center neonatal intensive care units and revision of empiric late-onset sepsis antibiotic prescribing guidelines

Alex Creevan, PharmD, Sara Clark, PharmD, Anavice Jimenez, PharmD Candidate, Michael Garcia, PharmD

PROVIDENCE Health & Services

Background

- Neonatal late-onset sepsis (LOS) is commonly defined as an infection occurring after the first 72 hours of life[1]. LOS is a common complication of prolonged admission to the neonatal intensive care unit (NICU) and is a major cause of morbidity and mortality.[2]
- Due to the risks associated with LOS, antibiotics are often started inappropriately in this population which can lead to multi-drug resistant bacteria, increased healthcare costs, alterations in the microbiome and an increased risk of necrotizing enterocolitis (NEC) and mortality.[3-5]
- Current Providence Oregon Regional empiric antibiotic guidelines for suspected LOS in the NICU do not provide clear prescribing recommendations, do not offer dosing recommendations, are likely underutilized by providers, and have not been updated since 2011. All of which could lead to inappropriate antibiotic prescribing.
- In October 2019, providers at two tertiary medical centers agreed upon using American Academy of Pediatrics (AAP) Red Book[6] for antibiotic dosing in neonates.

Purpose

- To retrospectively evaluate the appropriateness of antibiotic utilization in the NICU at two tertiary medical centers
- To promote standardization of antibiotic prescribing for LOS through revision of the 2011 regional empiric antibiotic guidelines for suspected LOS in the NICU

Objectives

Primary Objective:

- Measure and evaluate appropriateness of antibiotic utilization in the NICU at two tertiary medical centers and compare to the 2011 Providence Oregon regional guidelines and recommendations from neonatal antibiotic dosing references (AAP Red Book, Lexicomp[7], Neofax[8], or other)

Secondary Objective:

- Revision and implementation of new LOS guidelines (in process)

Methods

Study design: Retrospective chart review
Setting: Neonatal intensive care units at two tertiary healthcare facilities
Inclusion criteria:

- Admitted to the NICU at two tertiary medical centers
- Received at least one course of antibiotics starting after 72 hours of life

Exclusion criteria:

- Patients were excluded if inclusion criteria were not met

Results

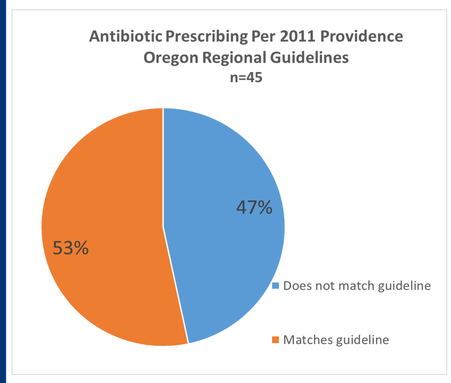
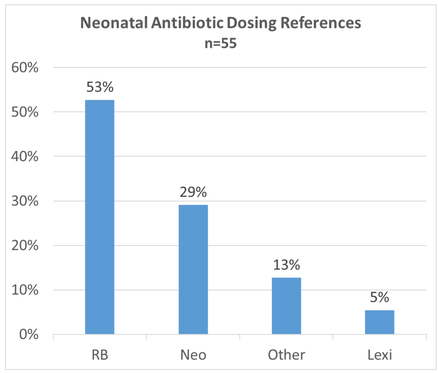


Figure 1. Antibiotic prescribing compared to 2011 Providence Oregon Regional Guidelines



RB = Red Book; Neo = Neofax; Lexi = Lexicomp

Figure 2. Neonatal antibiotic dosing reference utilization frequency after excluding antibiotics dosed by pharmacy

Characteristics n (%)	
Sex	n=35
Male	24 (69)
Site	n=35
NICU A	30 (86)
NICU B	5 (14)
Birthweight classification	n=35
ELBW (< 1000 g)	20 (57)
VLBW (< 1500 g)	7 (20)
LBW (< 2500 g)	7 (20)
Preterm birth category	n=35
EPT (< 28 weeks)	24 (69)
VPT (28-32 weeks)	5 (14)
MLPT (32-37 weeks)	5 (14)
Term (> 37 weeks)	1 (3)
Diagnosis	n=45
Presumed sepsis	15 (33)
Bacteremia	14 (31)
Presumed pneumonia	6 (13)
Bacterial pneumonia	5 (11)
Necrotizing enterocolitis	3 (7)
Viral meningitis	1 (2)
Viral pneumonia	1 (2)

ELBW = Extremely low birth weigh; VLBW = Very low birth weight; LBW = Low birth weight; EPT = Extremely preterm; VPT = Very preterm; MTLP = Moderate to late preterm

Table 1. Patient demographics

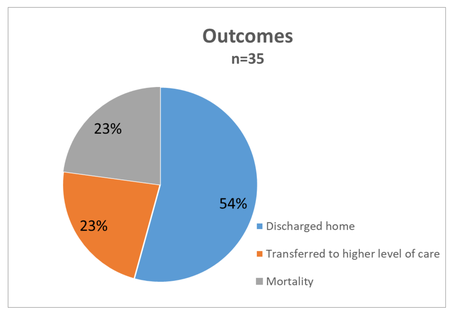


Figure 3. Patient outcomes at the end of NICU stay

Most Frequent Empiric Regimens n (%)	n=45
Gentamicin/nafcillin	11 (24)
Ceftazidime/vancomycin	6 (13)
Ampicillin/gentamicin	5 (11)
Ceftazidime/nafcillin	4 (9)
Cefepime/vancomycin	3 (7)

Table 2. Most frequently ordered empiric antibiotic regimens

Risk Factors n (%)	n=45
Central line	22 (49)
Total parenteral nutrition	23 (51)
	n=35
Previous IV antibiotics	25 (71)
Chronic lung disease	18 (51)
Patent ductus arteriosus	13 (37)
Maternal GBS status	n=35
Positive	8 (23)
Negative	12 (34)
Unknown	15 (43)
Respiratory support	n=35
Mechanical ventilation	17 (49)
Other	15 (43)
None	3 (9)

GBS =Group B *Streptococcus*

Table 3. Late-onset sepsis risk factors

Organism	
Blood	
GBS	4
E.coli	3
MSSA	2
Klebsiella pneumoniae	1
E. coli	1
Serratia marcescens	1
Enterococcus faecalis	1
Staph. hominis	1
CoNS	1
Klebsiella oxytoca	1
Respiratory	
Klebsiella oxytoca	3
MSSA	2
Serratia marcescens	1
E. coli	1
Klebsiella pneumoniae	1
Total	24

GBS = Group B *Streptococcus*; MSSA = methicillin susceptible *Staph. aureus*; CoNS = coagulase-negative *Staph.*

Table 4. Number of cultures stratified by organism and source

Conclusions

- There were 35 patients identified as having at least one occurrence of LOS, with 45 occurrences identified in total. After excluding antibiotics dosed by pharmacy (vancomycin and gentamicin), 55 antibiotics were evaluated based on neonatal antibiotic dosing reference.
- Nearly half (47%) of the empiric antibiotic regimes were not consistent with 2011 Regional guidelines. This variation is likely attributable to the vagueness of the guideline.
- Ampicillin and gentamicin were chosen as empiric antibiotics in 11% of empiric regimens.
  - Regional guidelines only recommend ampicillin and gentamicin for early-onset sepsis.
  - This was one factor that attributed to the high percentage of antibiotics categorized as "does not match guideline."
- While majority (53%) of dosing and/or dosing frequency of empiric antibiotics matched AAP Red Book, antibiotic dosing reference utilization was highly variable.
- For regimens in which Red Book was not utilized, the most frequently used dosing reference was Neofax at 29%, followed by "other" at 13%. Dosing was categorized as "other" if it did not match one of the specified dosing references. Lexicomp was used 5% of the time. It should be noted that Lexicomp frequently cites Red Book, and was only counted if the recommendation was not consistent with Red Book dosing.
- Prescribers would likely benefit from a standardized guideline for prescribing empiric antibiotics that includes dosing based on AAP Red Book recommendations.

Study Limitations:

- Retrospective, non-randomized study
- Small sample size

Next Steps

- Revision and implementation of new late-onset sepsis guidelines based on Red Book dosing recommendations

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Disclosures

DISCLOSURE: Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

- ***Alex Creevan: Nothing to disclose***
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